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Dear Norman:

I think the bone of contention we're chewing over will be fully macerated before much longer. I don't see how having three alleles itself helps much, since you might have successive developmental stages with, say, a pre-fetal, fetal and adult Hb without necessitating any biosynthetic relationships among them. However, Ingraham's analyses of Hb, Hb-S, etc. give some real foundation now for discussing one protein as a unit modification of another one. It will be interesting to see what fetal Hb turns out to be!

We have a gene in Salmonella, Ah_2^-, which inhibits the formation of phase -2 flagellar protein. So in Ah_2^+ you get one protein; in Ah_2^- you get another. But the specificity of protein-2 is determined at another (albeit linked) locus H_2. There is a whole flock of genes which regulate these alternatives, but may play no direct role in the specificity of the individual products. I believe, as you would, that the innumerable alleles of H_1 and H_2 respectively furnish this information, but I don't think this tells us much about protein synthesis.

So I still think purely genetic analysis may be giving the right answers but not necessarily on logically rigorous arguments. What's the point of arguing about it any longer when the biochemical evidence on mechanisms of protein biosynthesis is just around the corner.

I wish there could have been more discussion of Kossikov but the circumstances were very difficult. Any questions had to be submitted in writing (as the Russians knew no English!) and they were usually evaded. At one point K. had to admit he had not done very satisfactory reconstruction experiments on Suc^- — Suc^+.

Yours sincerely,

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Professor of Medical Genetics

JL/ew